UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,664	12/21/2000	Ayoub Rashtchian	IVGN 152.3 CON	7736

65482 7590 11/29/2007

INVITROGEN CORPORATION
C/O INTELLEVATE
P.O. BOX 52050
MINNEAPOLIS, MN 55402

EXAMINER
SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/741,664	RASHTCHIAN ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/17/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/17/2007 has been entered.

2. Currently, claim 60 is pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejection of claim 60 under 35 USC 112/2nd paragraph is withdrawn in view of the amendment to the claim. The claim now makes clear that the composition is stored at the recited temperature range.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 60 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

Claim 60 has been amended to recite in step (b) that nucleic acid molecules are added to the composition "such that said composition is not diluted more than 2x". The entire specification has been thoroughly reviewed but does not provide support for this amendment. The response cites page 17, lines 18-23 and page 22, lines 25-27 as support for the amendment. At page 17, lines 18-23, the specification generally teaches reagent compositions are provided in "ready to use concentrations, obviating the time consuming dilution and premixing steps necessary with previously available solutions". At page 22, lines 25-27, the specification teaches "once the reagent components have been obtained, they are mixed at working concentrations to form a solution suitable for immediate use with or without dilution…". However, the specification provides no support for the amendment such that "said composition is not diluted more than 2x". Accordingly, the amendment has introduced new matter into the claimed invention.

Claim Rejections - 35 USC § 103

7. Claim 60 is rejected under 35 USC 103(a) as being unpatentable over Holmes (WO 95/00664) in view of Gelfand (US Patent 5,618,703), Hoeltke (US Patent 5,814,502), and Scalice (US Patent 5,338,671).

Holmes teaches methods of performing multiple PCR reactions using different primer pair and templates to identify primer pairs suitable for detection of Salmonella species in samples (see para bridging pages 2-3; page 7, first full para; page 14, last para). Holmes teaches that the PCR reactions contained 105 uL comprising template DNA, 50mMKCL, 2.5 mM $MgCl_2$ (instant claim 26), 10 mM Tris, 200uM each dNTP (instant claim 28), 0.5% Tween, and 2.5 units of Taq

polymerase (23.8 U/ml). Holmes is silent with regard to the steps of making of the composition prior to template addition. Holmes does not teach storage of the composition at a range of -20°C to +4°C, a PCR reaction mix containing an antibody that binds to the thermostable enzyme, or additional of nucleic acids to the composition such that the composition is not diluted more than 2x.

However, it was well known to those of ordinary skill in the art at the time the invention was made, that a master mix is typically employed when performing multiple reactions in order to improve efficiency and consistency and to avoid pipetting error. For example, Gelfand teaches methods of performing multiple reverse transcription reactions wherein reagents, except nucleic acid molecules, are added in a master mix containing a thermostable polymerase, such as Taq, a nonionic detergent, all 4 dNTPs, and a buffer salt (see cols 27, lines 55-65; col 30 and col 31, lines 18-40). With regard to step (b) of claim 60, Gelfand specifically teaches a method wherein multiple samples were analyzed and "for consistency and to avoid pipetting errors" the mix was prepared as a master mix and aliquoted as 17 uL into different reaction tubes such that only a single uL of primer and 2 uL of template were added (see col. 31, lines 30-40) (therefore, the composition was not diluted more than 2x upon the addition of nucleic acid molecules). Further, Hoeltke specifically teaches making compositions containing pre-mixed reaction components in liquid form so that the user only has to add an aliquot of DNA in one single pipetting step (see col. 2, lines 20-22). Hoeltke teaches a composition which comprises a DNA polymerase, such as Taq, a buffering substance, a salt, and nucleoside triphosphates (see col 2,l ines 32-50). Hoeltke teaches that these compositions exhibit particularly high stability when stored between –20 and 4 deg C. Scalice teaches that the use of an antibody specific for a

thermostable DNA polymerase, such as Taq (cols 7-8), can be used to reduce or eliminate the formation of non specific products in PCR methods (see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the multiple PCR methods using different primers and template of Holmes with the use of a master mix, stored at a temperature between -20°C to +4°C, containing all reagents necessary for the reaction such that the methods could be performed requiring only contacting the PCR master mix with nucleic acid template and primers, as taught by Gelfand and Hoeltke, such that the master mix composition was not diluted more than 2x upon the addition of nucleic acid molecules as taught by Gelfand. The ordinary artisan would have been motivated to provide a master mix for the purpose of improving the consistency and to reduce pipetting errors in the reactions of Holmes, as taught by Gelfand. The ordinary artisan would have been motivated to store such compositions at a temperature between -20°C to +4°C because Hoeltke teaches that such compositions exhibit particular high stability when stored between -20°C to +4°C. In performing the improved methods of Holmes in view of Gelfand and Hoeltke, it would have been further prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a composition that further included at least one antibody that binds said thermostable polymerase in view of the teachings of Scalice . The ordinary artisan would have been motivated to add an antibody specific for Taq polymerase to the PCR master mix of Holmes in view of Gelfand and Hoeltke for the purpose of reducing the formation of non specific PCR products in the methods of Holmes because Scalice teaches that such antibody can be used to reduce or eliminate the formation of non specific products in PCR methods. The ordinary artisan would have been motivated to add the antibody to the PCR

master mixture of Holmes in view of Gelfand and Hoeltke for the purpose of providing necessary reagents in premixed form for use in any PCR reaction.

Response to Arguments

8. The response traverses the rejection. The response asserts that none of the references of Gelfand, Hoeltke, and Scalice teaches a master mix comprising a thermostable polymerase, a dNTP, an antibody that binds the polymerase, and a buffer salt, taken from a temperature between –20 and 4 deg C and then nucleic acid molecules are added to the mix such that it is not diluted more than 2x. The response then cites each reference individually, and asserts that the master mixes that Gelfand discloses lack a polymerase binding antibody, are assembled at room temperature before use and are diluted more than 2x upon use. This argument has been thoroughly reviewed but was not found persuasive. The Gelfand reference was not used to teach temperature of storage or a polymerase antibody. Further, Gelfand does illustrate and provide express motivation for the use of a master mix where all reagents are added together in a master mix expect for nucleic acid molecules, and wherein upon addition of nucleic acid molecules, the composition is not diluted more than 2x. Specifically, as noted in the rejection above, Gelfand teaches a composition wherein to 17 ul of a master mix, 1 ul of primer and 2ul of template are added. Gelfand teaches that the purpose of the master mix is to "for consistency and to avoid pipetting errors". Accordingly, Gelfand does teach a composition whose concentration is not diluted more than 2x upon the addition of nucleic acid molecules, as is recited in the instantly pending claims (see col. 31, lines 30-40). The response then asserts that although Hoeltke teaches master mixes are stable at the claimed temperature range, Hoeltke fails to disclose mixes containing a polymerase binding antibody and fails to disclose mixes that are not diluted more

than 2x by the addition of nucleic acid molecules. This argument has been thoroughly reviewed but was not found persuasive as the reference was not used for disclosure of disclose mixes containing a polymerase binding antibody or mixes that are not diluted more than 2x by the addition of nucleic acid molecules. Hoeltke, however, does provide ample motivation to store master mixes at the claimed temperature range and teaches the known method of storing master mixes at the claimed temperature range. The response then asserts that although Scalice teaches master mixes containing a polymerase binding antibody, it does not disclose storing at the claimed temperature range or a mix that is not diluted more than 2x by the addition of nucleic acids. This argument has been thoroughly reviewed but was not found persuasive as the reference was not used for disclosure of storing at the claimed temperature range or a mix that is not diluted more than 2x by the addition of nucleic acids. Scalice does provide ample motivation to use an polymerase binding antibody in PCR reactions, and teaches the known method of using a polymerase binding antibody in PCR reactions. The response is asserting that because each of the references does not individually teach each of the claimed limitations, that a prima facie case of obviousness has not been established. This is incorrect, as the standard being applied by the response is with regard to rejections under 35 USC 102, rather than 35 USC 103. There is absolutely no requirement that each individual reference must teach all of the claim limitations to satisfy 35 USC 103. Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The response has further ignored the teachings of motivation in each reference that would have been readily available to the ordinary artisan at the time the

invention was made. These express motivations would have provided ample direction to the ordinary artisan to arrive at the claimed method. Even absent these express teachings, the fact that each reference is in art analogous to the claimed method, and teach known and established techniques commonly used in the laboratory at the time the invention was made, render the claimed method obvious. The references teach techniques that improve methods and products in the same way.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays. NOTE: The examiner will be on maternity leave for a portion of December 2007 as well as the months of January and February 2008.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Jehanne Sitton/
Primary Examiner
Art Unit 1634
11/23/2007